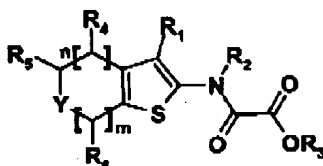


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CLAIM LISTING

1-109 (Cancelled)

110. (Currently amended) A compound of Formula 1



Formula 1

wherein

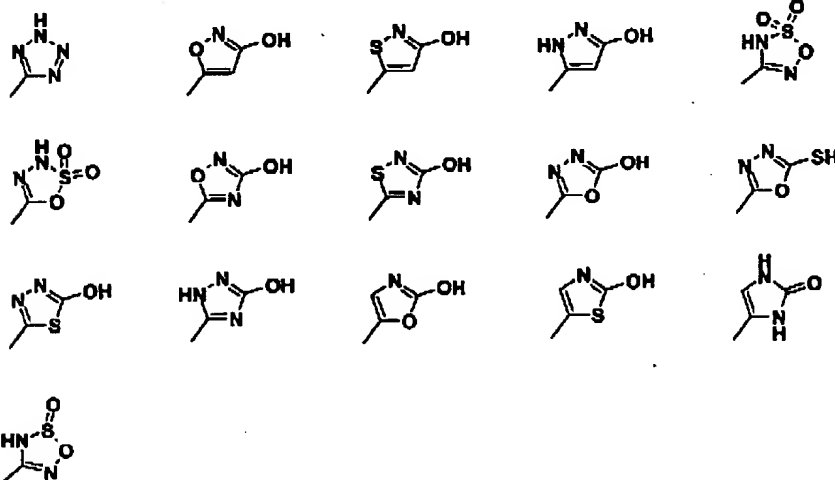
n is 1 or 2;

m is 1 or 2;

Y is O, SO or SO₂;

R₁ is COOH, COOC₁-C₆alkyl, COOarylC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl; ~~or a 5-membered heterocycles selected from the group consisting of:~~

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R₂ is hydrogen;

R₃ is hydrogen, C₁-C₆alkyl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyloxyC₁-C₆alkyl or C₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl;

R₄ is hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, provided R₄ does not represent a heterocyclic ring; wherein the alkyl and aryl groups are optionally substituted as defined below;

R₅ is hydrogen, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxycarbonyl, aryloxycarbonyl, arylC₁-C₆alkyloxycarbonyl, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxyC₁-C₆alkyl, arylC₁-C₆alkyloxyC₁-C₆alkyl, NR₇R₈, C₁-C₆alkylaminoC₁-C₆alkyl, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonyl-aminoC₁-C₆alkyl, -carbonylNR₈C₁-C₆alkylCOR₁₀, wherein R₁₀ is NR₇R₈ or C₁-C₆alkylNR₇R₈, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, CONR₇R₈, C₁-C₆alkylCONR₇R₈ or arylaminocarbonylaminoC₁-C₆alkyl, provided R₅ does not represent a heterocyclic ring; wherein the alkyl and aryl groups are optionally substituted as defined below;

R₆ is hydrogen, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxycarbonyl, aryloxycarbonyl, arylC₁-C₆alkyloxycarbonyl, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxyC₁-C₆alkyl, arylC₁-C₆alkyloxyC₁-C₆alkyl, NR₇R₈, C₁-C₆alkylaminoC₁-C₆alkyl, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, -carbonylNR₈C₁-C₆alkylCOR₁₀, wherein R₁₀ is NR₇R₈, or C₁-C₆alkylNR₇R₈, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, CONR₇R₈, or arylaminocarbonylaminoC₁-C₆alkyl; wherein the alkyl and aryl groups are optionally substituted as defined below;

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R₇ and R₈ are independently a saturated or partially saturated cyclic 5, 6 or 7 membered amine, imide or lactam or are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy wherein the alkyl and aryl groups are optionally substituted as defined below; or

R₇ and R₈ together with the nitrogen to which they are attached form a saturated, partially saturated or aromatic monocyclic, bicyclic or tricyclic ring system containing from 3 to 14 carbon atoms and from 0 to 3 additional heteroatoms selected from nitrogen, oxygen or sulphur, wherein the ring system is optionally substituted with at least one C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkyl-aminoC₁-C₆alkyl or NR₁₁R₁₂, wherein R₁₁ and R₁₂ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy, wherein the alkyl and aryl groups are optionally substituted as defined below;

wherein the optionally substituted alkyl groups are substituted with one or more groups independently selected from halo, cyano, nitro, trihalomethyl, carbamoyl, hydroxy, oxo, COOR₃, C₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, C₁-C₆alkylamino, arylamino, arylC₁-C₆alkylamino, di(arylC₁-C₆alkyl)amino, C₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy, arylcarboxy, arylC₁-C₆alkylcarboxy, C₁-C₆alkylcarbonylamino, -C₁-C₆alkylaminoCOR₁₃, wherein R₁₃ is C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy; arylC₁-C₆alkylcarbonylamino, tetrahydrofuranyl, morpholinyl, piperazinyl, or a saturated or partially saturated cyclic 5, 6 or 7 membered amine, imide or lactam, and

wherein the optionally substituted aryl groups are substituted with a group selected from halo, nitro, cyano, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylamino, C₁-C₆alkylaminoC₁-C₆alkyl, arylamino, arylC₁-C₆alkylamino, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-

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C₆alkylcarboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, arylC₁-C₆alkylcarbonylamino, or arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl;

or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, a racemic mixture, or any tautomeric form, or prodrug thereof.

111. (Previously presented) The compound according to claim 110, wherein R₁ is COOH, COOC₁-C₆alkyl, COOarylC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyC₁-C₆alkyl or COOC₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl.

112. (Previously presented) The compound according to claim 110, wherein n and m are 1.

113. (Previously presented) The compound according to claim 110, wherein Y is oxygen.

114. (Cancelled)

115. (Previously presented) The compound according to claim 110, wherein R₄ and R₆ are hydrogen.

116. (Previously presented) The compound according to claim 110, wherein R₆ is C₁-C₆alkylNR₇R₈.

117. (Previously presented) The compound according to claim 116, wherein R₇ is hydrogen and R₈ is arylC₁-C₆alkyl.

118. (Previously presented) The compound according to claim 117, wherein the aryl group is pyridyl.

119. (Previously presented) The compound according to claim 117, wherein the aryl group is phenyl optionally substituted with methoxy or CH₃(CO).

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120. (Previously presented) The compound according to claim 110, wherein R₆ is arylaminocarbonylaminoC₁-C₆alkyl.

121. (Previously presented) The compound according to claim 110, wherein R₆ is aryloxyC₁-C₆alkyl.

122. (Previously presented) The compound according to claim 121, wherein the aryl group is 1,1-dioxo-benzo[d]isothiazol-3-yl.

123. (Currently amended) ~~the~~ The compound according to claim 121, wherein the aryl group is 1,1-dioxo-5-phenyl-isothiazol-3-yl.

124. (Previously presented) The compound according to claim 121, wherein the aryl group is benzo[1,3]dioxol-5-yl.

125. (Previously presented) The compound according to claim 121, wherein the aryl group is 5-methoxy-2-methyl-1H-indol-3-yl.

126. (Previously presented) A composition comprising an effective amount of a compound of claim 110, together with one or more pharmaceutically acceptable carriers or diluents and an insulin sensitizer.

127. (Cancelled)

128. (Currently amended) A composition comprising an effective amount of a compound of claim 110, together with ~~one~~ one or more pharmaceutically acceptable carriers or diluents and an agent stimulating insulin release from β cells.

129. (Cancelled)

130. (Previously presented) A composition comprising a compound of claim 110, together with one or more pharmaceutically acceptable carriers or diluents and an antiobesity agent.

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131. (Cancelled)

132. (Previously presented) A composition according to claim 126, wherein the insulin sensitizer is a thiazolidinedione or a pharmaceutically acceptable salt thereof.

133. (Currently amended) A composition according to claim 126, wherein the insulin sensitizer is selected from troglitazone, ciglitazone, pioglitazone, rosiglitazone, 5-[4-[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione and 3-[4-[2-Phenoxazin-10-yl]ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable ~~salts~~ salt thereof.

134. (Previously presented) A composition according to claim 126, wherein the insulin sensitizer is (-) 3-[4-[2-Phenoxazin-10-yl]ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

135. (Cancelled)

136. (Cancelled)

137. (Cancelled)

138. (Previously presented) A composition according to claim 128, wherein the agent stimulating insulin release from β cells is repaglinide.

139. (Cancelled)

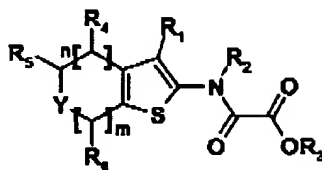
140. (Previously presented) A composition according to claim 130, wherein the antiobesity agent is orlistat.

141. (Cancelled)

142. (Cancelled)

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143. (Currently amended) A compound of Formula 1



Formula 1

wherein

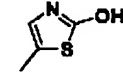
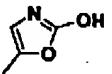
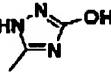
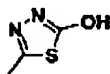
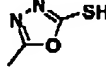
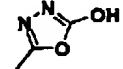
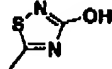
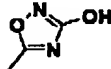
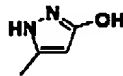
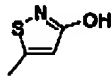
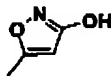
n is 1 or 2;

m is 1 or 2;

Y is O, S, SO or SO₂;

R₁ is COOH, COOC₁-C₆alkyl, COOarylC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl; ~~or a 5-membered heterocycle selected from the group consisting of:~~

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R₂ is hydrogen;

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R₃ is hydrogen, C₁-C₆alkyl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyloxyC₁-C₆alkyl or C₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl;

R₄ is hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, provided R₄ does not represent a heterocyclic ring; wherein the alkyl and aryl groups are optionally substituted as defined below;

R₅ is C₁-C₆alkylNR₇R₈ wherein R₇ and R₈ together with the nitrogen to which they are attached form a saturated, partially saturated or aromatic monocyclic, bicyclic or tricyclic ring system selected from the group consisting of pyrrolopyrazine, pyrrolopyridine, benzo[d]isoxazole, 1,1-dioxo-1,3-dihydro-benzo[d]isothiazole, pyrrolidine and 1,3-dihydro-benzo[d]isothiazole substituted with two oxo groups at the atom positions adjacent to the nitrogen atom, wherein the ring system is optionally be substituted with at least one C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, COOR₃, hydroxy, nitro, oxo, C₁-C₆alkyloxy, arylC₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylaminoC₁-C₆alkyl or NR₉R₁₀, wherein R₉ and R₁₀ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy; wherein the alkyl and aryl groups are optionally substituted as defined below;

wherein the optionally substituted alkyl groups are substituted with one or more groups independently selected from halo, cyano, nitro, trihalomethyl, carbamoyl, hydroxy, oxo, C₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, C₁-C₆alkylamino, arylamino, arylC₁-C₆alkylamino, di(arylC₁-C₆alkyl)amino, C₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy, arylcarboxy, arylC₁-C₆alkylcarboxy, C₁-C₆alkylcarbonylamino, -C₁-C₆alkylaminoCOR₁₃, wherein R₁₃ is C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkylcarbonylamino, tetrahydrofuranyl, morpholinyl, piperazinyl, or a saturated or partially saturated cyclic 5, 6 or 7 membered amine, imide or lactam, and

wherein the optionally substituted aryl group is substituted with a group selected from halo, nitro, cyano, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, COOR₃, , C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkyloxyC₁-

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C₆alkyl, C₁-C₆alkylamino, C₁-C₆alkylaminoC₁-C₆alkyl, arylamino, arylC₁-C₆alkylamino, arylC₁-C₆alkyl-aminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, carboxyC₁-C₆alkyloxy, C₁-C₆alkylcarbonylamino, C₆alkylaminoCOR₁₃, wherein R₁₃ is C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkylcarbonylamino or, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl;

R₆ is hydrogen;

or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, a racemic mixture, or any tautomeric form, or prodrug thereof.

144. (Previously presented) The compound according to claim 143, wherein the ring system is 1,3-dihydro-benzo[d]isothiazolyl, substituted with 2 oxo groups at the atom positions adjacent to the nitrogen atom.

145. (Previously presented) The compound according to claim 143, wherein the ring system is thiazolidin-2,4-dione.

146. (Previously presented) The compound according to claim 143, wherein the ring system is 5-(aryl-methyl)-thiazolidin-2,4-dione.

147. (Previously presented) The compound according to claim 143, wherein the ring system is pyrrolo[3,4-b]pyridine-5,7-dione.

148. (Previously presented) The compound according to claim 143, wherein the ring system is pyrrolo[3,4-b]pyridine-1,3-dione.

149. (Previously presented) The compound according to claim 143, wherein the ring system is pyrrolo[3,4-b]pyrazine-5,7-dione.

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150. (Previously presented) A composition comprising an effective amount of a compound of claim 143, together with one or more pharmaceutically acceptable carriers or diluents and an insulin sensitizer.

151. (Cancelled)

152. (Previously presented) A composition comprising an effective amount of a compound of claim 143, together with one or more pharmaceutically acceptable carriers or diluents and an agent stimulating insulin release from β cells.

153. (Cancelled)

154. (Previously presented) A composition comprising a compound of claim 143, together with one or more pharmaceutically acceptable carriers or diluents and an antiobesity agent.

155. (Cancelled)

156. (Previously presented) A composition according to claim 150, wherein the insulin sensitizer is a thiazolidinedione or a pharmaceutically acceptable salt thereof.

157. (Currently amended) A composition according to claim 150, wherein the insulin sensitizer ~~sensitizer~~ is selected from troglitazone, ciglitazone, pioglitazone, rosiglitazone, 5-[4-[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione and 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable ~~salts~~ salt thereof.

158. (Currently amended) A composition according to claim 150, wherein the insulin sensitizer is (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable ~~salts~~ salt thereof.

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159. (Cancelled)

160. (Cancelled)

161. (Cancelled)

162. (Previously presented) A composition according to claim 152, wherein the agent stimulating insulin release from β cells is repaglinide.

163. (Cancelled)

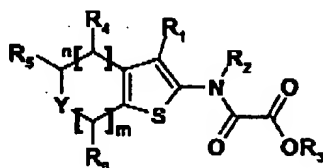
164. (Previously presented) A composition according to claim 154, wherein the antiobesity agent is orlistat.

165. (Cancelled)

166. (Cancelled)

167. (Currently amended) A compound of Formula 1

Formula 1



wherein

n is 1 or 2;

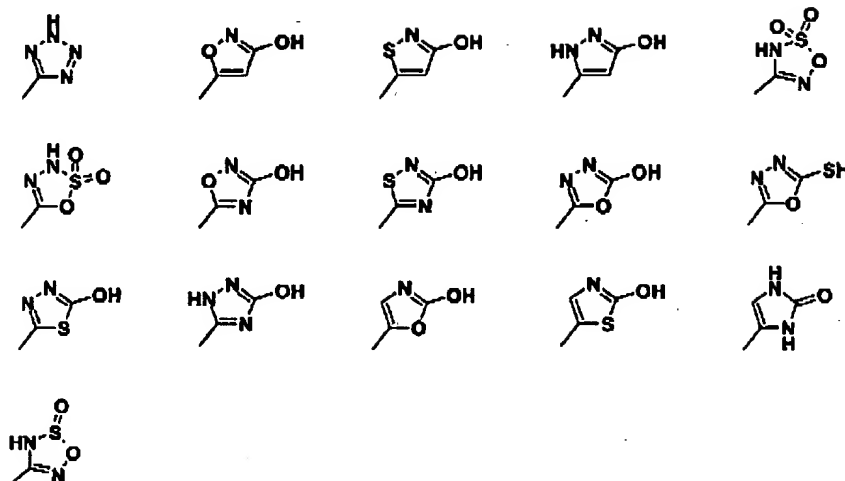
m is 1 or 2;

Y is O, S, SO or SO₂;

R₁ is COOH, COOC₁-C₆alkyl, COOarylC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl; or a 5-membered heterocycle selected from the group consisting of

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R₂ is hydrogen;

R₃ is hydrogen, C₁-C₆alkyl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyloxyC₁-C₆alkyl or C₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl;

R₄ is hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, provided R₄ does not represent a heterocyclic group; wherein the alkyl and aryl groups are optionally substituted as defined below;

R₅ is C₁-C₆alkylNR₇R₈ wherein R₇ and R₈ together with the nitrogen to which they are attached form isoindol wherein the ring system is optionally be substituted with at least one C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, fluoro, hydroxy, oxo, C₁-C₆alkyloxy, arylC₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylamino-C₁-C₆alkyl or NR₉R₁₀, wherein R₉ and R₁₀ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy; wherein the alkyl and aryl groups are optionally substituted as defined below or optionally substituted with one chloro or six chloros;

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wherein the optionally substituted alkyl groups are substituted with one or more groups independently selected from halo, cyano, nitro, trihalomethyl, carbamoyl, hydroxy, oxo, COOR₃, C₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, C₁-C₆alkylamino, arylamino, arylC₁-C₆alkylamino, di(arylC₁-C₆alkyl)amino, C₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy, arylcarboxy, arylC₁-C₆alkylcarboxy, C₁-C₆alkylcarbonylamino, -C₁-C₆alkylaminoCOR₁₂C₆alkylaminoCOR₁₃, wherein R₁₃ is C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkylcarbonylamino, tetrahydrofuranyl, morpholinyl, piperazinyl, , or a saturated or partially saturated cyclic 5, 6 or 7 membered amine, imide or lactam, and

wherein the optionally substituted aryl group is substituted with a group selected from halo, nitro, cyano, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, COOR₃, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylthio, arylC₁-C₆alkylthio, NR₇R₈, C₁-C₆alkylamino, C₁-C₆alkylaminoC₁-C₆alkyl, arylamino, arylC₁-C₆alkylamino, arylC₁-C₆alkyl-aminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, carboxyC₁-C₆alkyloxy, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -carbonylNR₇C₁-C₆alkylCOR₁₁,, wherein R₁₁ is C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl;

R₆ is hydrogen;

or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, a racemic mixture, or any tautomeric form, or prodrug thereof.

168. (Previously presented) The compound of claim 167, wherein the ring system is optionally substituted with hydroxy, nitro, methoxy, benzyloxy, fluoro, chloro CH₃CH₂CH₂NHC(O)- or CH₃C(O)NH.

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169. (Previously presented) A composition comprising an effective amount of a compound of claim 167, together with one or more pharmaceutically acceptable carriers or diluents and an insulin sensitizer.

170. (Cancelled)

171. (Previously presented) A composition comprising an effective amount of a compound of claim 167, together with one or more pharmaceutically acceptable carriers or diluents and an agent stimulating insulin release from β cells.

172. (Cancelled)

173. (Previously presented) A composition comprising a compound of claim 167, together with one or more pharmaceutically acceptable carriers or diluents and an antiobesity agent.

174. (Cancelled)

175. (Previously presented) A composition according to claim 169, wherein the insulin sensitizer is a thiazolidinedione or a pharmaceutically acceptable salt thereof.

176. (Currently amended) A composition according to claim 169, wherein the insulin ~~sensitizer~~ sensitizer is selected from troglitazone, ciglitazone, pioglitazone, rosiglitazone, 5-[4-[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione and 3-[4-[2-Phenoxazin-10-yl]ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable ~~salts~~ salt thereof.

177. (Currently amended) A composition according to claim 169, wherein the insulin sensitizer is (-) 3-[4-[2-Phenoxazin-10-yl]ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable ~~salts~~ salt thereof.

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178. (Cancelled)

179. (Cancelled)

180. (Cancelled)

181. (Previously presented) A composition according to claim 171, wherein the agent stimulating insulin release from β cells is repaglinide.

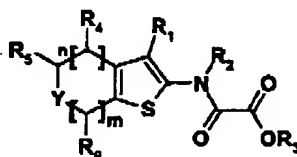
182. (Cancelled)

183. (Previously presented) A composition according to claim 173, wherein the antiobesity agent is orlistat.

184. (Cancelled)

185. (Cancelled)

186. (Currently amended) A compound of Formula 1



Formula 1

wherein

n is 1 or 2;

m is 1 or 2;

Y is O, S, SO or SO₂;

R₁ is COOH, COOC₁-C₆alkyl, COOarylC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl; or a 5-membered heterocycle selected from the group consisting of:

[[

Chemical structures of 15 pyrazole derivatives, numbered 1 to 15, showing various substituents and ring modifications:

- 1: 1,2,4-triazole-5-carbonitrile
- 2: 1,2,4-triazole-5-carbonitrile
- 3: 1,2,4-triazole-5-carbonitrile
- 4: 1,2,4-triazole-5-carbonitrile
- 5: 1,2,4-triazole-5-carbonitrile
- 6: 1,2,4-triazole-5-carbonitrile
- 7: 1,2,4-triazole-5-carbonitrile
- 8: 1,2,4-triazole-5-carbonitrile
- 9: 1,2,4-triazole-5-carbonitrile
- 10: 1,2,4-triazole-5-carbonitrile
- 11: 1,2,4-triazole-5-carbonitrile
- 12: 1,2,4-triazole-5-carbonitrile
- 13: 1,2,4-triazole-5-carbonitrile
- 14: 1,2,4-triazole-5-carbonitrile
- 15: 1,2,4-triazole-5-carbonitrile

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R₆ is hydrogen, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, oxo, carboxy, carboxyC₁-C₆alkyl, C₁-C₆alkyloxycarbonyl, aryloxycarbonyl, arylC₁-C₆alkyloxycarbonyl, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxyC₁-C₆alkyl, arylC₁-C₆alkyloxyC₁-C₆alkyl, NR₇R₈, C₁-C₆alkylaminoC₁-C₆alkyl, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -carbonylNR₈C₁-C₆alkylCOR₁₃, wherein R₁₃ is NR₇R₈, or C₁-C₆alkylNR₇R₈, arylC₁-

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C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, CONR₇R₈, C₁-C₆alkylCONR₇R₈ or arylaminocarbonylaminoC₁-C₆alkyl; wherein the alkyl and aryl groups are optionally substituted as defined below;

R₇ and R₈ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy wherein the alkyl and aryl groups are optionally substituted as defined below; or R₇ and R₈ are independently a saturated or partially saturated cyclic 5, 6 or 7 membered amine, imide or lactam;

wherein the optionally substituted alkyl groups are substituted with one or more groups independently selected from halo, cyano, nitro, trihalomethyl, carbamoyl, hydroxy, oxo, COOR₃, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, C₁-C₆alkylamino, arylamino, arylC₁-C₆alkylamino, di(arylC₁-C₆alkyl)amino, C₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy, arylcarboxy, arylC₁-C₆alkylcarboxy, C₁-C₆alkylcarbonylamino, -C₁-C₆alkylaminoCOR₁₃, wherein R₁₃ is C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkylcarbonylamino, tetrahydrofuranyl, morpholinyl, piperazinyl, or a saturated or partially saturated cyclic 5, 6 or 7 membered amine, imide or lactam; and

wherein the optionally substituted aryl group is substituted with a group selected from halo, nitro, cyano, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, COOR₃, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylthio, arylthio, arylC₁-C₆alkylthio, C₁-C₆alkylamino, C₁-C₆alkylaminoC₁-C₆alkyl, arylamino, arylC₁-C₆alkylamino, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, arylC₁-C₆alkylcarboxy, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl;

or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, a racemic mixture, or any tautomeric form, or prodrug thereof.

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187. (Previously presented) The compound according to claim 186, wherein R_1 is COOH, COOC₁-C₆alkyl, COOarylC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl.

188. (Previously presented) The compound according to claim 186, wherein n and m are 1.

189. (Previously presented) The compound according to claim 186, wherein Y is oxygen.

190. (Cancelled)

191. (Previously presented) The compound according to claim 186, wherein R_4 and R_6 are hydrogen.

192. (Previously presented) The compound according to claim 186, wherein R_6 is C₁-C₆alkylNR₇R₈.

193. (Previously presented) The compound according to claim 192, wherein R_7 is hydrogen and R_8 is arylC₁-C₆alkyl.

194. (Previously presented) The compound according to claim 193, wherein the aryl group is pyridyl.

195. (Previously presented) The compound according to claim 193, wherein the aryl group is phenyl optionally substituted with methoxy or CH₃C(O).

196. (Previously presented) The compound according to claim 186, wherein R_6 is arylaminocarbonylaminoC₁-C₆alkyl.

197. (Previously presented) The compound according to claim 186, wherein R_6 is aryloxyC₁-C₆alkyl.

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198. (Previously presented) The compound according to claim 197, wherein the aryl group is 1,1-dioxo-benzo[d]isothiazol-3-yl.

199. (Currently amended) ~~the~~ The compound according to claim 197, wherein the aryl group is 1,1-dioxo-5-phenyl-isothiazol-3-yl.

200. (Previously presented) The compound according to claim 197, wherein the aryl group is benzo[1,3]dioxol-5-yl.

201. (Previously presented) The compound according to claim 197, wherein the aryl group is 5-methoxy-2-methyl-1H-indol-3-yl.

202. (Previously presented) A composition comprising an effective amount of a compound of claim 186, together with one or more pharmaceutically acceptable carriers or diluents and an insulin sensitizer.

203. (Cancelled)

204. (Previously presented) A composition comprising an effective amount of a compound of claim 186, together with one or more pharmaceutically acceptable carriers or diluents and an agent stimulating insulin release from β cells.

205. (Cancelled)

206. (Previously presented) A composition comprising a compound of claim 186, together with one or more pharmaceutically acceptable carriers or diluents and an antiobesity agent.

207. (Cancelled)

208. (Previously presented) A composition according to claim 202, wherein the insulin sensitizer is a thiazolidinedione or a pharmaceutically acceptable salt thereof.

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209. (Currently amended) A composition according to claim 202, wherein the insulin ~~sensitizer~~ sensitizer is selected from troglitazone, ciglitazone, pioglitazone, rosiglitazone, 5-[[4-[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione and 3-[4-[2-Phenoxazin-10-yl]ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable ~~sales~~ salt thereof.

210. (Previously presented) A composition according to claim 202, wherein the insulin sensitizer is (-) 3-[4-[2-Phenoxazin-10-yl]ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

211. (Cancelled)

212. (Cancelled)

213. (Cancelled)

214. (Previously presented) A composition according to claim 204, wherein the agent stimulating insulin release from β cells is repaglinide.

215. (Cancelled)

216. (Previously presented) A composition according to claim 206, wherein the antiobesity agent is orlistat.

217. (Cancelled)

218. (Cancelled)

219. (Previously presented) A compound which acts as an inhibitor of Protein Tyrosine Phosphatases selected from the group consisting of

2-(Oxalyl-amino) (1,1,3-trioxo-1,3-dihydro-1H-benzo[d]isothiazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran carboxylic acid;

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5-(4-Chloro-1,3-dioxo-1,3-dihydro-isoindol-2-yl-methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4,5,6,7-Tetrachloro-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Methoxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-Hydroxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-Benzoyloxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-Fluoro-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(1,3-Dioxo-1,3-dihydro-benzo[f]isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Acetylamino-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-Acetylamino-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5,7-Dioxo-5,7-dihydro-pyrrolo[3,4-b]pyrazin-6-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(5,7-Dioxo-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5,7-Dioxo-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-ylmethyl)-2-(oxalylamino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5,7-Dioxo-5,7-dihydro-pyrrolo[3,4-c]pyridin-6-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Nitro-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Hydroxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-Methoxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl) (oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

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5-(4-Nitro-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-(4-Chloro-phenylsulfanyl)-6-methyl-1,3-dioxo-1,3-dihydro-pyrrolo[3,4-c]pyridin-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(3-Imidazol-1-yl-2,5-dioxo-pyrrolidin-1-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

Oxalic acid 3-carboxy-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-5-ylmethyl ester methyl;

Oxalic acid (3-carboxy-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-5-ylmethyl) ester;

7-Hydroxymethyl-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(2,4-Dioxo-thiazolidin-3-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(1,3-Dioxo-1,3-dihydro-isoindol-2-ylloxymethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(4-Hydroxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Methoxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(5,7-Dioxo-5,7-dihydro-[1,3]dioxolo[4,5-f]isoindol-6-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(((Benzo[1,3]dioxole carbonyl)amino)methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(3-(2,4-Dimethoxy-phenyl)ureidomethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-5-phenylcarbonyl-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-Benzylcarbonyl-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3,7-dicarboxylic acid 7-ethyl ester;

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7-Benzylcarbamoyl-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-((2-(4-Methanesulfonyl-phenyl)-acetylamino)-methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-((3-Carboxy-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-5-ylmethyl)-carbamoyl)nicotinic acid;

7-(2,4-Dioxo-5-pyridin-2-ylmethylene-thiazolidin-3-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(2,4-Dioxo-5-pyridin-ylmethyl-thiazolidin-3-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(5-(4-Methoxy-benzylidene)-2,4-dioxo-thiazolidin-3-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(5-(4-Acetylamino-benzylidene)-2,4-dioxo-thiazolidin-3-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(5-(3,5-Dimethoxy-benzylidene)-2,4-dioxo-thiazolidin-3-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-[5-(1H-Imidazol-4(5)-ylmethylene)-2,4-dioxo-thiazolidin-3-ylmethyl]-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(1,3-Dioxo-4,7-epoxido-1,3,4,5,6,7-hexahydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(((2R)-Amino-3-phenyl-propionylamino)methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-((2-Acetylamino-3-(4-hydroxy-phenyl)-propionylamino)methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-((2-Acetylamino-3-methyl-butyrylamino)methyl)-3-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-7-(1,1,3-trioxo-1,3-dihydro-1H-benzo[d]isothiazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-7-(1,1,3-trioxo-1H-benzo[d]isothiazol-3-yloxomethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-7-(3-oxo-3H-benzo[d]isoxazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

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2-(Oxalyl-amino)-7-(1,1,3-trioxo-5-phenyl-1,3-dihydro-isothiazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(1,1-Dioxo-5-phenyl-1H-isothiazol-3-ylloxymethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-5-(1,1,3-trioxo-5-phenyl-1,3-dihydro-isothiazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(1,1-Dioxo-5-phenyl-1H-isothiazol-3-ylloxymethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(6-Chloro-1,1,3-trioxo-2,3-dihydro-4H-thieno[3,2-e]-1,2,4-thiadiazin-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(6-Chloro-1,1-dioxo-4H-thieno[3,2-e]-1,2,4-thiadiazine-3-ylloxymethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(1,3-Dioxo-1,3-dihydro-benzo[d]isothiazol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran carboxylic acid;

5-(1,3-Dioxo-1,3-dihydro-benzo[d]isothiazol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Benzyl-1,1-dioxo-[1,2,5]thiadiazolidin-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Ethyl-1,1-dioxo-[1,2,5]thiadiazolidin-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-7-(1-oxo-1,3-dihydro-isoindol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-5-(2,2,2-trifluoro-acetoxymethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(((Benzo[1,3]dioxol-5-ylmethyl)-amino)methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-((2-Methoxy-benzylamino)methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-((2-Benzo[1,3]dioxol-yl-acetylamino)methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(((5-Methoxy-2-methyl-1H-indol-3-carbonyl)amino)methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

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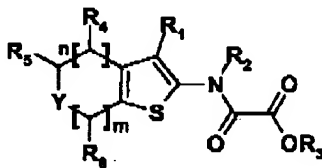
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5-(1,3-Dioxo-5-propylcarbamoyl-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;
or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, including a racemic mixture, or any tautomeric form, or prodrug thereof.

220. (Currently amended) A compound of Formula 1



Formula 1

wherein

n is 1 or 2;

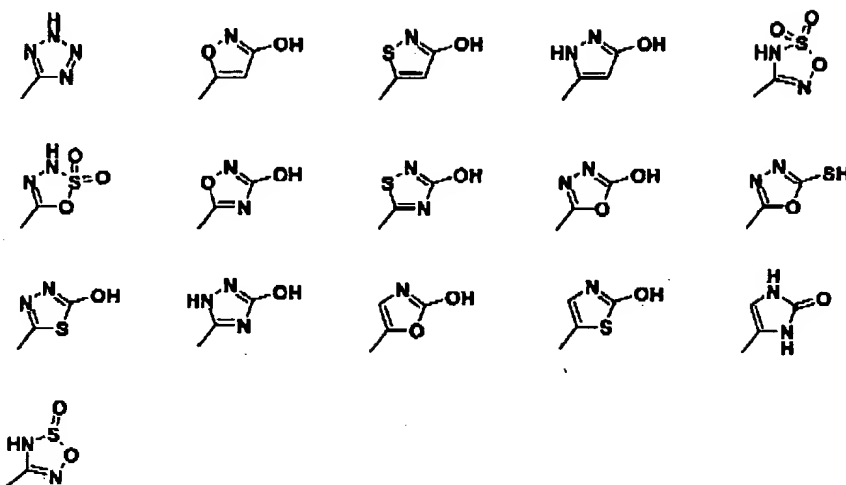
m is 1 or 2;

Y is O, S, SO or SO₂;

R₁ is COOH, COOC₁-C₆alkyl, COOarylC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl; ~~or a 5-membered heterocycles selected from the group consisting of:~~

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II

R₂ is hydrogen;

R₃ is hydrogen, C₁-C₆alkyl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyloxyC₁-C₆alkyl or C₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl;

R₄ is hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, provided R₄ does not represent a heterocyclic ring; wherein the alkyl and aryl groups are optionally substituted as defined below;

R₅ is hydrogen, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxycarbonyl, aryloxycarbonyl, arylC₁-C₆alkyloxycarbonyl, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxyC₁-C₆alkyl, arylC₁-C₆alkyloxyC₁-C₆alkyl, NR₇R₈, C₁-C₆alkylaminoC₁-C₆alkyl, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonyl-aminoC₁-C₆alkyl, -carbonylNR₈C₁-C₆alkylCOR₁₀, wherein R₁₀ is NR₇R₈, or C₁-C₆alkylNR₇R₈, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, CONR₇R₈, C₁-C₆alkylCONR₇R₈ or arylaminocarbonylaminoC₁-C₆alkyl, provided R₅ does not represent a heterocyclic ring; wherein the alkyl and aryl groups are optionally substituted as defined below and;

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R₆ is trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxycarbonyl, aryloxycarbonyl, arylC₁-C₆alkyloxycarbonyl, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxyC₁-C₆alkyl, arylC₁-C₆alkyloxyC₁-C₆alkyl, NR₇R₈, C₁-C₆alkylaminoC₁-C₆alkyl, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, carbonylNR₈C₁-C₆alkylCOR₁₀, wherein R₁₀ is NR₇R₈, or C₁-C₆alkylNR₇R₈, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, CONR₇R₈, or arylaminocarbonylaminoC₁-C₆alkyl; wherein the alkyl and aryl groups are optionally substituted as defined below and;

R₇ and R₈ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy, a saturated or partially saturated cyclic 5, 6 or 7 membered amine, imide or lactam, or

R₇ and R₈ together with the nitrogen to which they are attached form a saturated, partially saturated or aromatic monocyclic, bicyclic or tricyclic ring system containing from 3 to 14 carbon atoms and from 0 to 3 additional heteroatoms selected from nitrogen, oxygen or sulphur, wherein the ring system is optionally substituted with at least one C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkyl-aminoC₁-C₆alkyl or NR₁₁R₁₂, wherein R₁₁ and R₁₂ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy; wherein the alkyl and aryl groups are optionally substituted as defined below,

wherein the optionally substituted alkyl groups are substituted with one or more groups independently selected from halo, cyano, nitro, trihalomethyl, carbamoyl, hydroxy, oxo, COOR₃, C₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, C₁-C₆alkylamino, arylamino, arylC₁-C₆alkylamino, di(arylC₁-C₆alkyl)amino, C₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy, arylcarboxy, arylC₁-C₆alkylcarboxy, C₁-C₆alkylcarbonylamino, -C₁-C₆alkylaminoCOR₁₃, wherein R₁₃ is C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkylcarbonylamino, tetrahydrofuranyl, morpholinyl,

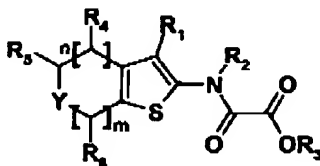
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piperazinyl, or a saturated or partially saturated cyclic 5, 6 or 7 membered amine, imide or lactam;

and wherein the optionally substituted aryl group is substituted with a group selected from halo, nitro, cyano, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylamino, C₁-C₆alkylaminoC₁-C₆alkyl, arylamino, arylC₁-C₆alkylamino, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl;

or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, a racemic mixture, or any tautomeric form, or prodrug thereof.

221. (Currently amended) A compound of Formula 1



Formula 1

wherein

n is 1 or 2;

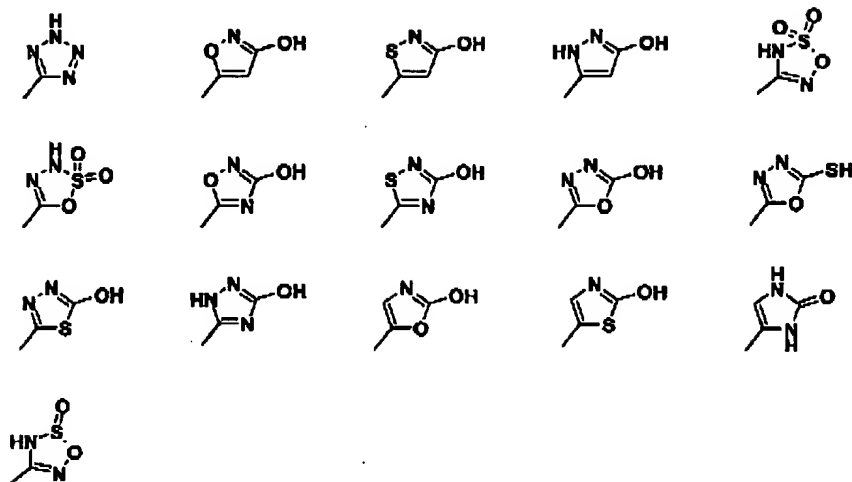
m is 1 or 2;

Y is O, S, SO or SO₂;

R₁ is COOH, COOC₁-C₆alkyl, COOarylC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl; ~~or a 5-membered heterocycles selected from the group consisting of:~~

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R₂ is hydrogen;

R₃ is hydrogen, C₁-C₆alkyl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyloxyC₁-C₆alkyl or C₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl;

R₄ is hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, provided R₄ does not represent a heterocyclic ring; wherein the alkyl and aryl groups are optionally substituted as defined below;

R₅ is trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxycarbonyl, aryloxycarbonyl, arylC₁-C₆alkyloxycarbonyl, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxyC₁-C₆alkyl, arylC₁-C₆alkyloxyC₁-C₆alkyl, NR₇R₈, C₁-C₆alkylaminoC₁-C₆alkyl, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonyl-aminoC₁-C₆alkyl, -carbonylNR₈C₁-C₆alkylCOR₁₀, wherein R₁₀ is NR₇R₈, or C₁-C₆alkylNR₇R₈, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, CONR₇R₈, C₁-C₆alkylCONR₇R₈ or

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arylamino-carbonylamino-C₁-C₆alkyl, provided R₅ does not represent a heterocyclic ring;
wherein the alkyl and aryl groups are optionally substituted as defined below and;

R₆ is hydrogen, trihalomethyl, C₁-C₆alkyl, aryl, aryl-C₁-C₆alkyl, C₁-C₆alkyloxycarbonyl, aryloxycarbonyl, aryl-C₁-C₆alkyloxycarbonyl, C₁-C₆alkyloxy, C₁-C₆alkyloxy-C₁-C₆alkyl, aryloxy-C₁-C₆alkyl, aryl-C₁-C₆alkyloxy-C₁-C₆alkyl, NR₇R₈, C₁-C₆alkylamino-C₁-C₆alkyl, aryl-C₁-C₆alkylamino-C₁-C₆alkyl, di(aryl-C₁-C₆alkyl)amino-C₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonyl-C₁-C₆alkyl, aryl-C₁-C₆alkylcarbonyl, aryl-C₁-C₆alkylcarbonyl-C₁-C₆alkyl, C₁-C₆alkylcarboxy-C₁-C₆alkyl, arylcarboxy-C₁-C₆alkyl, aryl-C₁-C₆alkylcarboxy-C₁-C₆alkyl, C₁-C₆alkylcarbonylamino, carbonyl-NR₈-C₁-C₆alkyl-COR₁₀, wherein R₁₀ is NR₇R₈, or C₁-C₆alkyl-NR₇R₈, aryl-C₁-C₆alkylcarbonylamino, aryl-C₁-C₆alkylcarbonylamino-C₁-C₆alkyl, CONR₇R₈, or arylaminocarbonylamino-C₁-C₆alkyl; wherein the alkyl and aryl groups are optionally substituted as defined below and;

R₇ and R₈ are independently selected from hydrogen, C₁-C₆alkyl, aryl, aryl-C₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or aryl-C₁-C₆alkylcarboxy, a saturated or partially saturated cyclic 5, 6 or 7 membered amine, imide or lactam, or

R₇ and R₈ together with the nitrogen to which they are attached form a saturated, partially saturated or aromatic monocyclic, bicyclic or tricyclic ring system containing from 3 to 14 carbon atoms and from 0 to 3 additional heteroatoms selected from nitrogen, oxygen or sulphur, wherein the ring system is optionally substituted with at least one C₁-C₆alkyl, aryl, aryl-C₁-C₆alkyl, hydroxy, C₁-C₆alkyloxy, C₁-C₆alkyloxy-C₁-C₆alkyl, C₁-C₆alkyl-amino-C₁-C₆alkyl or NR₁₁R₁₂, wherein R₁₁ and R₁₂ are independently selected from hydrogen, C₁-C₆alkyl, aryl, aryl-C₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, aryl-C₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or aryl-C₁-C₆alkylcarboxy; wherein the alkyl and aryl groups are optionally substituted as defined below;

wherein the optionally substituted alkyl groups are substituted with one or more groups independently selected from halo, cyano, nitro, trihalomethyl, carbamoyl, hydroxy, oxo, COOR₃, C₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, aryl-C₁-C₆alkyloxy, C₁-C₆alkylamino, arylamino, aryl-C₁-C₆alkylamino, di(aryl-C₁-C₆alkyl)amino, C₁-C₆alkylcarbonyl, aryl-C₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy, arylcarboxy, aryl-C₁-C₆alkylcarboxy, C₁-C₆alkylcarbonylamino, -C₁-

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C₆alkylaminoCOR₁₃, wherein R₁₃ is C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkylcarbonylamino, tetrahydrofuranyl, morpholinyl, piperazinyl, or a saturated or partially saturated cyclic 5, 6 or 7 membered amine, imide or lactam;

and wherein the optionally substituted aryl group is substituted with a group selected from halo, nitro, cyano, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylamino, C₁-C₆alkylaminoC₁-C₆alkyl, arylamino, arylC₁-C₆alkylamino, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl;

or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, a racemic mixture, or any tautomeric form, or prodrug thereof.